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SYSTEMATIC REVIEW

Efficacy of acupuncture on fibromyalgia syndrome: a Meta-analysis

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Abstract

OBJECTIVE: To comprehensively evaluate the effectiveness of acupuncture as a treatment for fibromyalgia syndrome.

METHODS: Two review authors independently selected the trials for the Meta-analysis, assessed their methodological quality and extracted relevant data. A quality assessment was conducted according to the Cochrane Review Handbook 5.0. RevMan 5.0.20 software was used in the statistical analysis.

RESULTS: A total of 523 trials were reviewed and 9 trials were selected for Meta-analysis. (a) Compared acupuncture with sham acupuncture, there was a significant difference in the visual analogue scale, but no difference in the pressure pain threshold. Additionally, and there was a difference in the fibromyalgia impact questionnaire and the multidisciplinary pain inventory after 4 weeks of treatment, but no difference after 7 weeks of therapy. There was no difference in the numerical rating scale in weeks 3, 8 and 13. (b) Acupuncture versus drugs. There were differences in the VAS after 20 days of acupuncture and moxibustion treatment comparing with the drug amitriptyline, and after 4 weeks of acupuncture and moxibustion treatment comparing with the drug fluoxetine and amitriptyline. There were also differences in the number of tender points when comparing acupuncture with amitriptyline or fluoxetine. There was no difference in total efficiency when comparing acupuncture with amitriptyline after 4 weeks of treatment, but there were differences between the two groups 45 days after treatment. There were also differences in total efficiency comparing acupuncture with fluoxetine, and when comparing 4 weeks post-treatment of acupuncture with a combination of amitriptyline, oryzanol and vitamin B. (c) A comparison of acupuncture, drugs and exercise with drugs and exercise showed PPT differences in months 3 and 6. There was no difference between the two comparison groups after follow-up visits in months 12 and 24.

CONCLUSION: Compared with sham acupuncture, there was not enough evidence to prove the efficacy of acupuncture therapy for the treatment of fibromyalgia. Some evidence testified that the effectiveness of acupuncture therapy for fibromyalgia was superior to drugs; however, the included trials were not of high quality or had high bias risks. Acupuncture combined with drugs and exercise could increase pain thresholds in the short term, but there is a need for higher quality randomized controlled trials to further confirm this.

Key words: Acupuncture; Fibromyalgia; Meta-analysis; Randomized controlled trial; Controlled clinical trial

INTRODUCTION

Fibromyalgia syndrome (FMS) is a non-joint rheumatism, that clinically mainly manifests as diffused skeletal muscle pain and systemic symmetrical distributed tender points,[1] accompanied by symptoms such as fatigue, depression, anxiety, dipsomania, headaches, diffuse abdominal pain, and frequent micturition that severely affect the patient's quality of life.[2,3] To date, there are no domestic epidemiology statistics for this disorder. The American Rheumatism Association (ARA) states that FMS is the third most common rheumatic disease, after rheumatoid arthritis (RA) and osteoarthritis (OA).[4] The incidence of FMS is approximately 2%-4% with a female to male gender ratio of approximately 9∶1.[5-6] The predilection age focuses on 35-50[7] and the pathogenesis is not yet known.[8-10] A study indicated that kinship to patients with FMS means a higher susceptibility, suggesting it is related to both genes and environmental factors.[11]

The European League Against Rheumatism (EULAR) currently regards the drug amitriptyline as the most effective for FMS treatment, but its side effects hinder its use as a long-term therapeutic method. As an economical therapeutic method, however, acupuncture and moxibustion have been used to treat pain syndrome for more than 2000 years.[12] Studies suggest that 60%-90% of FMS patients use one or more complementary or alternative therapeutic methods;[13,14] of these 22% try acupuncture and moxibustion therapy.[15] FMS therapeutic guidelines moderately recommend acupuncture and moxibustion as they may improve FMS symptoms.[16,17]

A systematic review and Meta-analysis can insure the quality of a specialized-recommendation therapeutic schedule that has superior clinical directive significance. At present, China's clinical trials do not include international systematic reviews[15,18,19] on acupuncture versus sham acupuncture interventions whose results reveal no evidence verifying that acupuncture therapy achieves better results than sham acupuncture. Similarly, domestic systematic reviews[20] that demonstrate that interventions achieve better results than amitriptyline in the treatment of FMS are not included in international clinical trials.These reviews all had methodological limitations and were published prior to 2010. Hence, the current study thoroughly researched the randomized and quasi-randomized controlled trials both in China and abroad. On the basis of systematic reviews, outcome indicators were chosen that objectively reflected the clinical curative effect and presented the overall evaluation for clinical efficacy of acupuncture versus placebo and Western Medicine as well as acupuncture comprehensive therapy.

METHODS

Eligibility criteria

The research type: the chosen trials were either randomized controlled trials (RCT) or controlled clinical trials (CCT). CCT did not comply strictly with the random distribution method. For example, the distribution was in accordance with admission sequence or other not-genuine randomized methods. The language was limited to Chinese and English.

The research objects: there were no limits to research subjects' age, gender, treatment courses, or source. The definite diagnostic criteria were in line with FMS diagnostic criteria established by the American College of Rheumatology (ACR) in 1990.[21]

The intervention types: the treatment group received acupuncture therapy (no limits in needle type, needle size and needle amounts, acupoint prescriptions, operating techniques, needle retention time, and course of treatment); the control groups received sham acupuncture (nonpoints were stimulated and not stimulated on the surface of the skin) or took Western Medicine (no limits in type and dose). In addition, the treatment group which received acupuncture combined with the certain therapy and the control group with the same certain therapy were both included. The acupuncture therapy included filiform needle acupuncture, electro-acupuncture (EA), moxibustion, laser irradiation, and point application.

The outcome indicators: the major outcome indicators were a visual analogue scale (VAS), and a numerical rating scale (NRS). The minor outcome indicators were: the number of tender points (TePsN), the pressure pain threshold (PPT), the short-form health survey (SF-36), the fibromyalgia impact questionnaire (FIQ), the multidisciplinary pain inventory (MPI), and the total efficacy rate.

Information sources

Information was sourced by electronic retrieval from Chinese databases such as China National Knowledge Infrastructure Database (1979-2012), China Science and Technology Journal Database (1989-2012), Wanfang Database (1998-2012), and from the English databases PubMed (1966-2012), EMBASE (1980-2012) and Cochrane Library (fourth issue, 2012). Data were also manually retrieved by searching library back issues and recently published literature not contained in the above databases.

Search strategy

The Chinese search terms used were: 'acupuncture and moxibustion', 'needling' and 'fibromyalgia'. The English search terms were: 'fibromyalgia', 'fibromyal*', and 'acupuncture'. The period searched was until March 1, 2012. The specific retrieval strategy was:

To locate FMS: #1 fibromyalgia [MeSH]; #2 fibromyal* [tw]; #3 OR/1-2.

To locate acupuncture interventions: #4 acupuncture [MeSH]; #5 acupuncture therapy [MeSH]; #6 acupuncture points [MeSH]; #7 body acupuncture [tw]; # 8 electroacupuncture [MeSH]; #9 electro-acupuncture [tw]; #10 electrical acupuncture [tw]; #11 ear acupuncture [MeSH]; #12 auricular acupuncture [tw]; #13 scalp acupuncture [tw]; #14 OR/4-13; #15 3 AND 14.

Data extraction

Two evaluators independently reviewed each study title and abstract. After excluding studies that clearly did not meet the inclusion criteria, the remaining trials were read in full for further determination. The reviewers cross-checked the test results and differences in opinions were resolved by discussion or by third party arbitration.

Risk of bias in individual studies

Following the quality assessment standard recommended by the Cochrane Review Handbook 5.0,[22] the bias risk assessment tool involved six aspects: (a) random distribution method; (b) allocative decision concealment; (c) whether the research objects, therapeutic plan operators, and those measuring the results were blinded; (d) result integrity; (e) presenting the study findings selectively; and (f) other bias resources. Each research result was examined based on the above six aspects and judged as "YES" (low-degree bias), "NO" (high-degree bias) or "unclear" (lacking relative information or uncertain bias condition). Two evaluators cross-verified the quality assessment results of the inclusive trials and differences in opinions were resolved by discussion or by third party arbitration.

Summary measures and synthesis of results

Data Meta-analysis was conducted using RevMan 5.0.20 software,[23] Each chosen study was tested for heterogeneity, and was considered heterogeneous if $P<0.1$ or $I^2>50\%$. A fixed effect model was used if no statistical heterogeneity existed in each study; if heterogeneity existed, its origin was established. If clinical or methodological heterogeneity did not exist, a random effect model was employed. Descriptive analysis was used if distinct clinical heterogeneity existed in each study. Weighted mean difference (*WMD*) was used for continuous variables, relative risk (*RR*) for categorical variables, and a 95% confidence interval (*CI*) signified every effect size, with $P\leq0.05$ being judged to have a statistical significant meaning.

Risk of bias across studies and additional analyses

Subgroup analysis: to inspect the relationship between acupuncture therapeutic efficacy and the therapeutic course.

Sensitivity analysis: to check the stability of the results and exclude lower-quality literature (unclear allocation concealment) and trials with over 20% drop out rate.

Publication bias: applying RevMan software[23] to evaluate publication bias (over 10 trials at minimum).

Dealing with missing data: the trial author was contacted when the mean or standard deviation was absent. If the data remained unavailable, the standard deviation was estimated through standard error, *P*-value, *t*-value, or the mean was replaced with the median if the original data was under a normal distribution.

RESULTS

Study selection

In total, 677 relevant articles were identified: 551 of these met the inclusive criterion, and 126 duplicated articles were excluded. Articles from Chinese journals in English, non-English language literature, systematic reviews, literature reviews, case reports, and specialists' experience were excluded, leaving a total of 52 articles. The full text of these was carefully reviewed with only nine final articles being selected for Meta-analysis (reasons for exclusion: 10 case observations, 10 repetitive articles, seven non-randomized controlled trials, 15 other intervention models, and one without original data). Data collection process as shown in Figure 1.

Study characteristics

Research type: of the nine final studies, six[24-27,30,32] were RCT and three[28,29,31] were CCT.

Research object: of the nine articles, one[29] did not mention the patient source, four[27,28,30,31] dealt with outpatients and/or inpatients, and the remaining four[24-26,32] studied recruited patients. All nine trials were in line with the diagnostic criteria established by the ARA in 1990.

Research interventions: in the trial test groups, two studies[24,25] used EA, one[31] used transcutaneous electrical stimulation, one[27] applied laser irradiation to acupuncture points, one[32] employed acupuncture combined with antidepressant drugs and exercise, and the remaining four treated with acupuncture. In the trial control groups, three trials[27,28,31] used amitriptyline, one[29] used fluoxetine, one[30] used amitriptyline with the oryzanol and vitamin B1, three[24-26] used sham acupuncture, and one[32] used antidepressants with exercise (Table 1).

The selected acupuncture points: one trial[25] chose the points based on acupuncture and moxibustion literature, two trials[27,28] adopted clinical experiences combined with the theory of Chinese medicine point selection, and the others employed Chinese medical theory point selection (Table 2).

Risk of bias within studies

Random allocation method: four trials[24-26,32] used computers to generate the random allocation sequence, one[30] used a random number table to generate the random sequence, one used the ballots method,[27] and the others[28,29,31] were randomized sequences according to the date of attending the doctor.

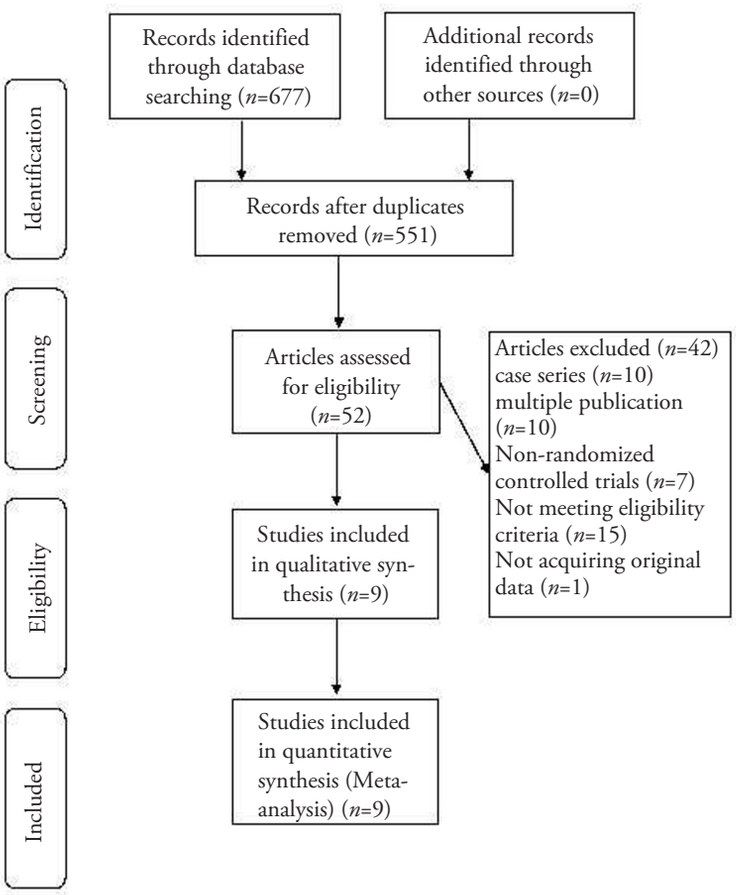

Figure 1 Flow chart of report selection process

Allocation concealment: two trials[24,26] used allocation concealment and the others did not describe it.

Blinding method: two trials[25,26] used blinding methods, and the remainder did not describe whether they did.

Selective research report: one trial[31] had a selective research report bias risk, the report of a further trial[29] was not clearly depicted, and the other trials had no selective report bias.

Other bias sources: only one trial[26] stated that it had no other bias risk; the others did not determine whether there were other bias sources. The specific bias analysis of each test is shown in Figures 2 and 3.

Synthesis of results

Acupuncture *vs* sham acupuncture: evaluation of VAS pain scale: One trial[24] was included to contrast EA and sham acupuncture groups based on the difference in curative effect, using the VAS pain scale. After 3 weeks of treatment, the measured outcomes showed that the two groups had statistically significant VAS score differences [*WMD*= - 13.89, 95% *CI* (- 28.86, - 0.92)].

PPT scale score: Martin DP *et al* [25] was included to contrast EA and sham acupuncture groups based on the difference in curative effect, using the PPT scale. After 3 weeks of treatment, the measured outcomes showed that the two groups had no statistically significant PPT score differences [*WMD*=0.78, 95% *CI* (0.01, 1.55)].

FIQ scale evaluation: one trial[25] was included to contrast ordinary acupuncture and sham acupuncture groups based on the difference in curative effect, using the FIQ scale. After 4 weeks of treatment, the measured outcomes revealed that the two groups had statistically significant FIQ scale differences [*WMD*= - 7.40, 95% *CI* (- 13.60, - 1.20)]. After 7 weeks of treatment, the results showed that the two groups had no statistically significant FIQ score differences [*WMD*= - 4.60, 95% *CI* (- 10.65, 1.45)].

MPI scale evaluation: one trial[25] was included to contrast ordinary acupuncture and sham acupuncture groups based on the difference in curative effect, using the MPI scale. After 4 weeks of treatment, the measured outcomes revealed that the two groups had statistically significant MPI score differences [*WMD*= - 7.40, 95% *CI* (- 13.12, - 1.68)]. After 7 weeks of treatment, the results showed that the two groups had no statistically significant MPI score differences [*WMD*= - 4.10, 95% *CI* (- 10.20, 2.00)].

NRS scale evaluation: two trials[26a/b] (a/b: one article includes two different trials) were included to contrast ordinary acupuncture and sham acupuncture groups based on the difference in curative effect. An NRS scale evaluation was employed in weeks 3, 8 and 13. The combined results in week 3 revealed that the two groups had no statistically significant NRS score difference [*WMD*= - 1.06, 95% *CI* (- 10.41, - 8.30), Chi^2=0.03, I^2=0%]. The combined results in week 8 showed the two groups had no statistically significant

Table 1 Main study characteristics

Study	Intervention		Course of treatment	Main outcome
	Experimental intervention	Control intervention		
Deluze C *et al* 1992[24]	Electro-acupuncture (*n*=36)	Sham acupuncture (*n*=34)	3 weeks (2 treatment/week)	- VAS - PPT
Martin DP *et al* 2006[25]	Electro-acupuncture (*n*=25)	Sham acupuncture (*n*=25)	4, 28 weeks (1 treatment/2 to 4 days during 2 to 3 weeks)	- FIQ - MPI
Harria RE *et al* 2005a[26]	Traditional Chinese acupuncture (*n*=25)	Nontraditional site with stimulation (*n*=28)	- 3 weeks: 1 treatment/week - 3 weeks: 2 treatment/week	- NRS (pain intensity) - MFI (fatigue)
Harria RE *et al* 2005b[26]	Traditional Chinese acupuncture (*n*=25)	Nontraditional site with no stimulation (*n*=27)	- 3 weeks: 3 treatment/week	- SF-36 (PF)
Wang CM 2008[27]	Traditional Chinese acupuncture together with acupoint laser irradiation (*n*=28)	Amitriptyline (*n*=28)	20 days	- VAS
Guo AS *et al* 2005[28]	Traditional Chinese acupuncture (*n*=19)	Amitriptyline (*n*=19)	4 weeks	- VAS - TePsN - Total efficiency
Guo Y *et al* 2010[29]	Electro-acupuncture together with TDP (*n*=36)	Fluoxetine (*n*=35)	4 weeks	- VAS - TePsN - Total efficiency
Wang SP *et al* 2002[30]	Traditional Chinese acupuncture (*n*=28)	Amitriptyline together with Oryzanol and Vitamin B1 (*n*=28)	4 weeks	- MPQ (PRI, PPI) - Total efficiency
Guo XJ *et al* 2004a[31]	Dermal neurological electrical stimulation (*n*=22)	Amitriptyline (*n*=22)	45 days	- Total efficiency
Guo XJ *et al* 2004b[31]	Chinese electro-acupuncture (*n*=22)	Amitriptyline (*n*=22)		
Targino RA *et al* 2008[32]	Traditional Chinese acupuncture together with tricyclic antidepressants and exercise (*n*=34)	tricyclic antidepressants and exercise (*n*=24)	12, 24, 48, 96 weeks (2 treatment/week)	- VAS - TePsN - PPT - SF-36 (PF, RP, BP, GH, VT, SF, RE, MH)

Notes: a/b: one article includes two different trials. VAS: visual analogue scale; PPT: pressure pain threshold; FIQ: fibromyalgia impact questionnaire; MPI: multidisciplinary pain inventory; NRS: numerical rating scale; MFI: multi-dimensional fatigue inventory; SF-36: short-form health survey (PF: physical functioning, RP: role physical, BP: bodily pain, GH: general health, VT: vitality, SF: social functioning, RE: role emotional, MH: mental health); TePsN: the number of tender points; TDP: specific electromagnetic spectrum treatment device; MPQ: McGill pain questionnaire (PRI: pain rating index, PPI: present pain intensity).

NRS score differences [*WMD*= - 6.80, 95% *CI* (- 3.66, 17.25), Chi^2=1.17, I^2=15%]. The combined results in week 13 showed the two groups had no statistically significant NRS score differences [*WMD*=4.19, 95% *CI* (- 6.86,15.24) Chi^2= 0.75, I^2=0%] (Figure 4).

Acupuncture versus drugs

VAS pain scale: all three included acupuncture versus drugs trials[27-29] used the VAS pain scale. Two of these compared the efficacy of acupuncture with amitriptyline: one[27] of which measured the outcome on day 20 to reveal that the two groups had statistically significant VAS score differences [*WMD*= - 2.27, 95% *CI* (- 3.05, - 1.49)] and the other[28] of which measured the outcome in week 4 showing that the two groups had statistically significant VAS score differences [*WMD*= - 17.10, 95% *CI* (- 23.93, - 10.27)]. The third trial[29] compared the efficacy of acupuncture therapy with fluoxetine and measured the outcome in week 4 showing that the two groups had statistically significant VAS score difference [*WMD*= - 2.47, 95% *CI* (- 3.13, - 1.81)] (Figure 5).

Evaluation of TePsN (the number of tender points)

Two included trials[28,29] investigated TePsN, and a TePsN tender point count was conducted after 4 weeks of treatment in both. One trial[28] compared acupuncture with amitriptyline, and the result proved that the two groups had statistically significant TePsN differences [*WMD*= - 4.00, 95% *CI* (- 6.73, - 1.27)]. The other trial[29] contrasted the efficacy of acupuncture therapy with fluoxetine, and the result revealed that the two groups had statistically significant TePsN differences [*WMD*= - 5.20, 95% *CI* (- 7.78, - 2.62)].

Evaluation of total efficiency: five trials[28-30,31a/b] investigating total efficiency were included. Three trials[28,31a/b] compared acupuncture with amitriptyline, one[28] of which measured the treatment outcome after 4 weeks showing that the two groups had no statistically significant differences in the case of total efficacy [*RR*=1.38, 95% *CI* (1.00, 1.91)]. The other two trials[31a/b] adopted the same indicators of efficacy and measured the out-

Table 2 Summary of treatment acupuncture points and rationale for selection of acupuncture points

Study	Acupuncture points	Rationale for selection of acupuncture points	Adverse event
Martin DP *et al* 2006[25]	Hegu (LI 4), Zusanli (ST 36), Xingjian (LR 2), Sanyinjiao (SP 6), Shenmen (HT 7)	Acupuncture literature	None (+)
Harria RE *et al* 2005a/b[26]	Baihui (GV 20), Shangyang (LI 11), Hegu (LI 4), Yanglingquan (GB 34), Zusanli (ST 36), Sanyinjiao (SP 6), Sanjian (LI 3)	TCM theory	Mild bruising and soreness Mild vasovagal symptoms
Wang CM 2008[27]	Ahshi-point	TCM theory Clinical experience	Not mentioned
Guo AS *et al* 2005[28]	Points of Governor Vessel, Urinary Bladder Meridian of Foot-Taiyang, the first and second lateral line	TCM theory Clinical experience	Not mentioned
Guo Y *et al* 2010[29]	Ahshi-point Adjunct points: Pishu (BL 20), Weishu (BL 21), Zusanli (ST 36), Hegu (LI 4), Jiexi (ST 41), Quchi (LI 11), Sanyinjiao (SP 6), Guanyuan (CV 4), Shenshu (BL 23), Shenmen (HT 7), Geshu (BL 17), Fengmen (BL 12), Waiguan (TE 5), Taichong (LR 3)	TCM theory	Palpitation 0/6 (treatment group/control group) Mouth dryness 0/8 Dizziness 0/4 Perspiration 0/5 In appetence 0/4 Constipation 0/2
Wang SP *et al* 2002[30]	Ahshi-point Shaoshang (LU 11), Taiyuan (LU 9), Shangyang (LI 1), Sanjian (LI 3)	TCM theory	Not mentioned
Guo XJ *et al* 2004a/b[31]	Main point: Fenchi (GB 20), Jianjing (GB 21), Xinshu (BL 15), Dushu (BL 16), Geshu (BL 17), Zhibian (BL 54), Huantiao (GB 30), Huiyang (BL 35), Quchi (LI 11), Ququan (LR 8), Kufang (ST 15), Wuyi (ST 14) Adjunct points: Taixi (KI 3), Shenmen (HT 7), Zusanli (ST 36), Neiguan (PC 6)	TCM theory	Not mentioned
Targino RA *et al* 2008[32]	Hegu (LI 4), Zusanli (ST 36), Xingjian (LR 2), Sanyinjiao (SP 6), Neiguan (PC 6), Yanglingquan (GB 34)	TCM theory	Not mentioned

Notes: a/b: one article includes two different trials. TCM: Traditional Chinese Medicine.

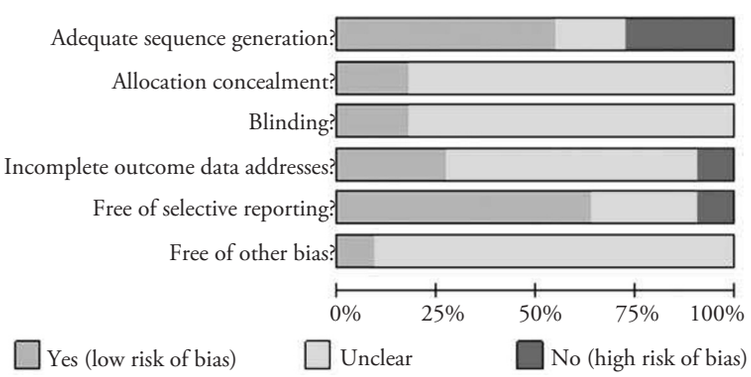

Figure 2 Each methodological quality item presented as percentages across all included studies

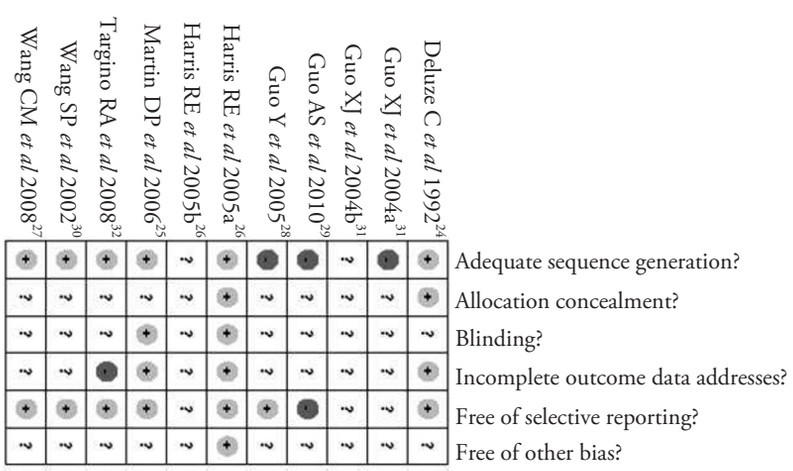

Figure 3 Each risk of bias domain for each included study

come after 45 days of treatment. Their combined results showed that the two groups had statistically significant differences for total efficacy [*RR*=1.43, 95% *CI* (1.16, 1.76), Chi^2=0.03, I^2=0%]. One trial[29] compared the efficacy of acupuncture with fluoxetine after 4 weeks of treatment, and the results showed that the two groups had statistically significant differences for total efficacy [*RR*=1.60, 95% *CI* (1.18, 2.17)]. One trial[30] compared the efficacy of acupuncture with amitriptyline, oryzanol and vitamin B after 4 weeks of treatment, and the results showed that the two groups had a statistically significant difference [*RR*=1.50, 95% *CI* (1.13, 1.99)] (Figure 6).

Acupuncture, drugs and exercise vs Western Medicine and exercise

Only one trial[32] compared the efficacy of acupuncture, antidepressants and exercise with antidepressants and exercise. In this study, only the PPT scores were analyzed and the results showed a statistically significant difference in both the first 3 months [*WMD*=0.69, 95% *CI* (0.38, 1.00)] and 6 months [*WMD*=0.57, 95% *CI* (0.25, 0.89)]. There was no statistically significant difference on follow-ups in months 12 and 24 (Figure 7).

Risk of bias across studies and additional analyses

Subgroup analysis. Comparing acupuncture with sham acupuncture, there were significant effects on the MPI and FIQ scores after 4 weeks of acupuncture treatment; however, there were no effects on MPI and FIQ scores after 7 weeks of acupuncture treatment. Comparing acupuncture with Western Medicine (amitriptylin): after 4 weeks of acupuncture treatment there were no effects on total efficacy; however, after 45 days, there were significant effects.

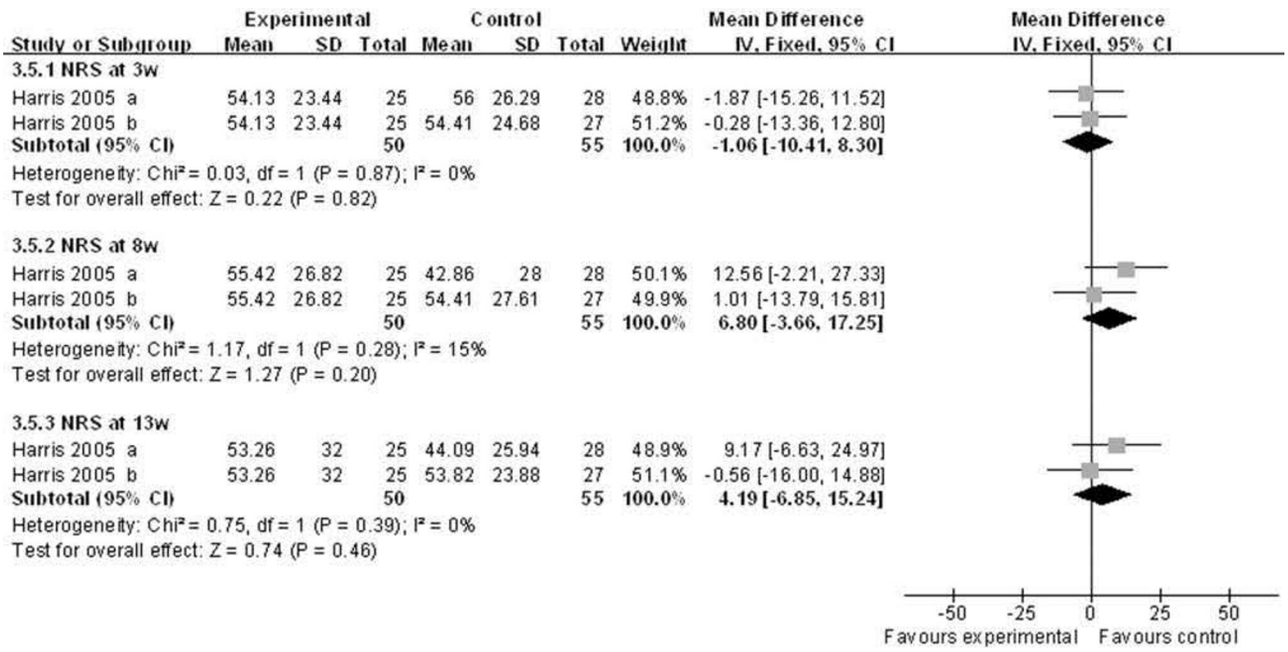

Figure 4 Meta-analysis of efficacy on acupuncture *vs* sham acupuncture by numerical rating scale

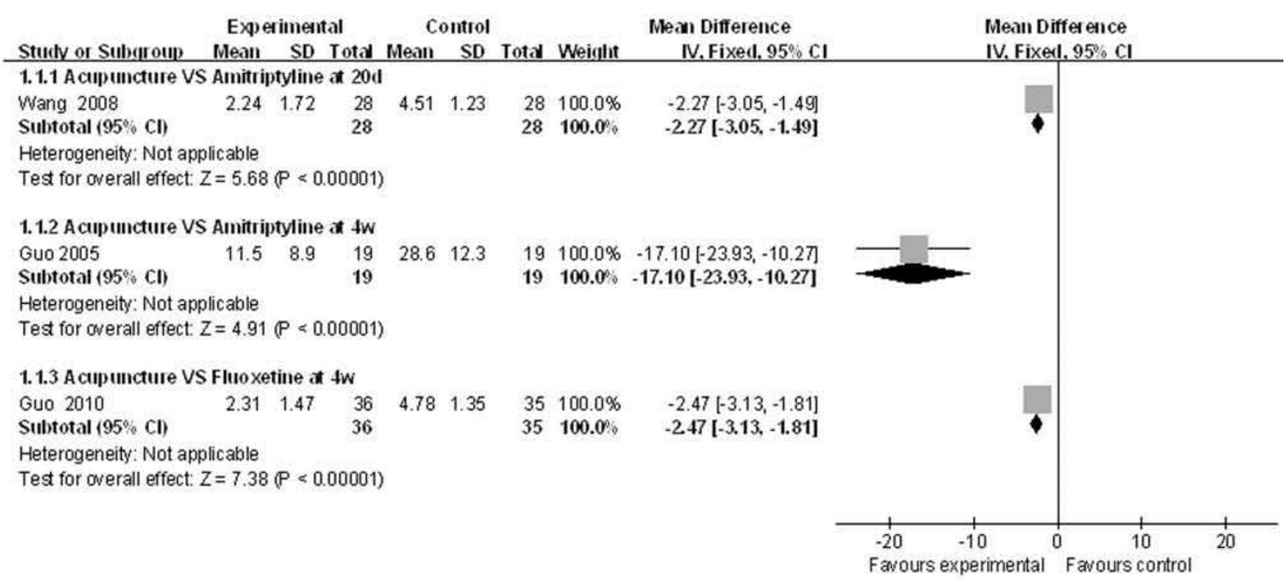

Figure 5 Meta-analysis of efficacy on acupuncture *vs* drugs by visual analogue scale

Sensitivity Analysis. There was no significant heterogeneity in the NRS scale evaluation outcomes in weeks 3, 8 and 13. Because of the limited number of studies, the potential sources of heterogeneity could not be assessed.

Publication bias. Because less than 10 studies were analyzed, a visual inspection of funnel plots for indicators of publication bias was not undertaken.

Dealing with missing data. The VAS, TePsN, and SF-36 data in one trial[32] were all median, and it was

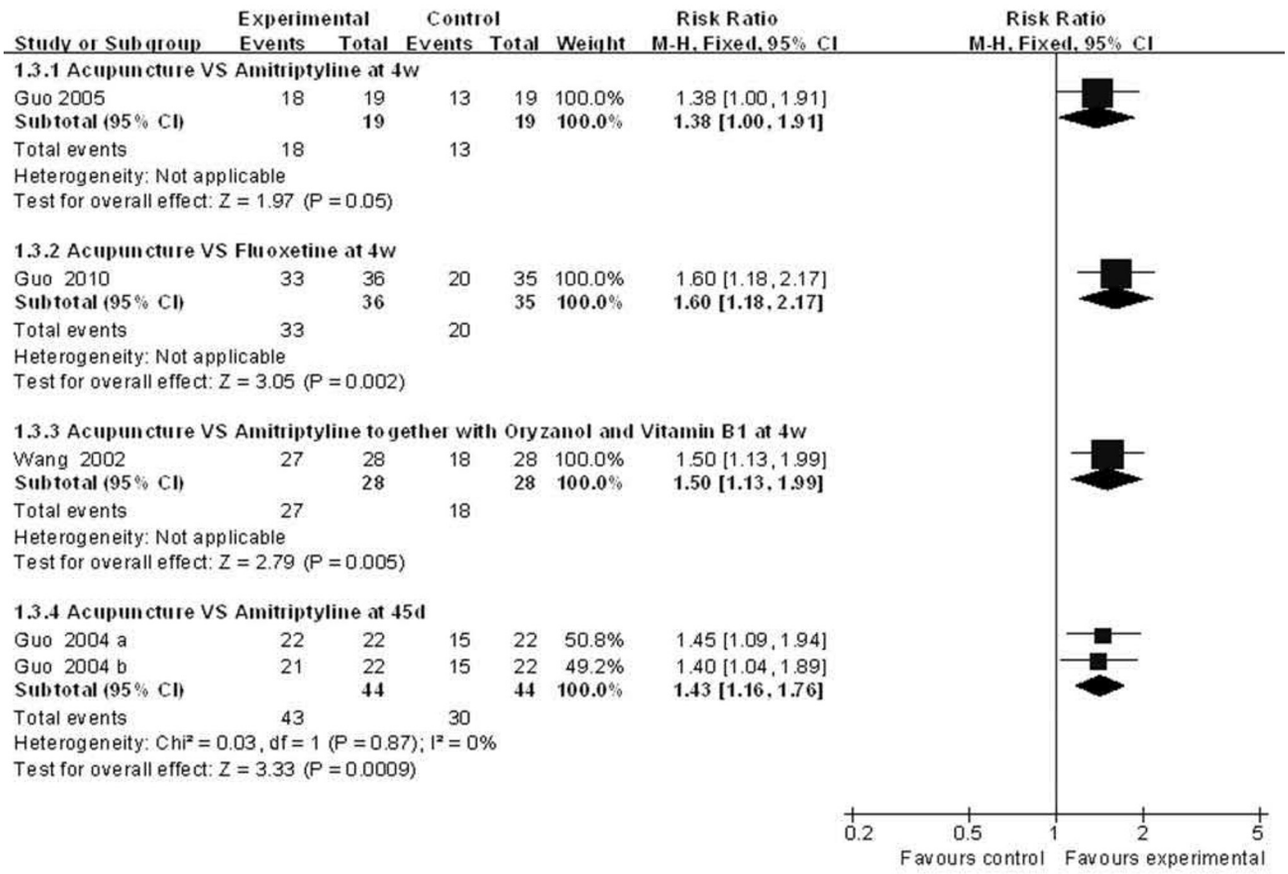

Figure 6 Meta-analysis of efficacy on acupuncture *vs* drugs by total efficacy rate

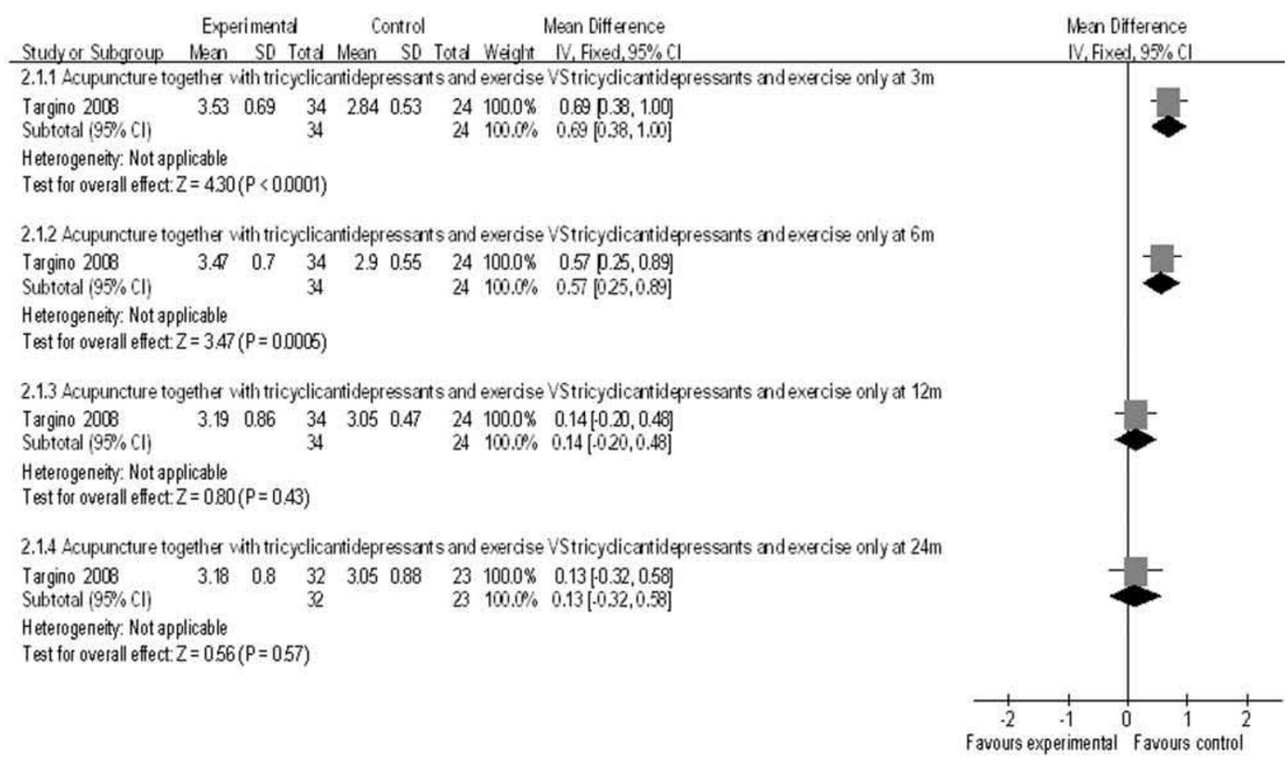

Figure 7 Meta-analysis of efficacy on acupuncture + drugs+ exercise *vs* drugs + exercise by pressure pain threshold

not possible to establish the original data or to determine whether it was a normal distribution, thus the median was not equivalent to the mean. Only the PPT scores were analyzed in this case.

DISCUSSION

Summary of evidence

In conclusion, there was not sufficient evidence to prove that acupuncture had advantages in the treatment of FMS compared with sham acupuncture. However, for pain relief and reducing the number of tender points, acupuncture proved superior to drugs. Because of the high risk of bias from low-quality literature, high quality RCT trials are needed to support the conclusion. Moreover, there is evidence that pain thresholds can increase with a combination of acupuncture, Western Medicine and exercise in the short run (3-6 months), but there was no evidence of advantages in the long run follow-up period (12-24 months).

Methodological strengths and limitations of included trials

Comparing acupuncture with antidepressant was undertaken in five clinical trials in China but without foreign reports. Meta-analysis results have shown the superiority of acupuncture in the treatment of FMS. However, measurement bias was likely as there was no allocation concealment or blinding in the included research. Moreover, there was a baseline imbalance because of the selection bias led by quasi-randomized control trials in some included trials.[28-30] It was not possible to increase test efficiency by less combined data. The blinding method was one of the 22 recommended items in the CONSORT statement;[33] however, it was difficult to implement because of the strong operability of acupuncture. This is also one of the reasons for the low-quality of acupuncture literature. Therefore, the present authors stress the importance of double-blinding for the trial subject and outcome operator and of blind assessment in blind acupuncture trials.[34,35] For instance, researchers could blindfold patients and prevent the trial subject from talking with others who have accepted the acupuncture therapy to implement blinding and reduce the risk of bias.[25,26] With regard to measuring the total effective rate, the trials applied varied measurement standards without clear sources leading to weak powers of test and specificity. Thus, the authenticity of the results needs to be proved by further rigorous clinical trials.

Despite the methodology limitations, the superiority of acupuncture in the treatment of FMS cannot be denied. A systematic review[36] of a RCT trial comparing amitriptyline and sham acupuncture suggested statistical significance after a 6-8 week period of taking drugs in the aspect of relieving pain and fatigue; however, no significance in week 12 revealed the short-lived superiority of amitriptyline. The present findings suggested that acupuncture was superior to amitriptyline on days 20, 28 and 45, further certifying the superiority of acupuncture.

Four of the trials[24,25,26a/b] comparing acupuncture and sham acupuncture had a high methodological quality; however, three[24,26a/b] chose points away from the verum acupoint for the sham acupuncture group and had a negative result. The authors of this current paper consider this to be incorrect because (a) they may have punctured other meridians or acupoints and thus generated certain therapeutic effects, (b) it is difficult to find a true ineffective acupoint,[37] (c) the width of the meridians was unclear, thus whether the sham acupoint was on the verum meridian could not be established, and (d) it was not possible to establish if the acupoints chosen in the trials were of superior efficiency because there is a lack of generally accepted superior acupoint groups. In addition, the Meta-analysis revealed a general trend: there was statistical significance in the VAS, FIQ, and MPI scales in weeks 3 and 4, but this became negative after week 4. Therefore, there is a need to establish if this difference was caused by the effect of acupuncture or the scales on their own.

Aerobic exercise and anti-depressant drug recommended by American Pain Society was the evidence-based A-level while acupuncture was C-level.[38] However, in one trial[32] the effect of acupuncture was prominent when the acupuncture, aerobic exercise and anti-depressant drug therapies were integrated, particularly in the third month. Although blinding and allocation concealment were not described in the trial, acupuncture would be the main therapy rather than other therapies with its increasing therapeutic effect if the integrated therapy was proven by more trials.[39]

In addition, the advantage of using acupuncture to treat FMS was the low number of side effects. Three RCTs[25,26,29] assessed the adverse events of acupuncture treatment. Acupuncture side effects were mild[26] and infrequent[25] compared with sham acupuncture, and when compared with drug treatment, no severe adverse acupuncture effects were noted.[29] Applying acupuncture for the management of FMS might result in fewer adverse effects than drug treatments.

Limitations of the systematic review and Meta-analysis

The Chinese literature included in this systematic review was of a generally low quality and there was a high risk of bias from some of the quasi-randomized control trials. Moreover, a small sample had a high bias potential owing to the effect of certain elements. A focus on subgroup analysis, less combined data, and weak test power were likely to generate false positive conclusions. Therefore conclusions should be treated cautiously. Moreover, there was a certain clinical heterogeneity because of differences in acupoint application, course of treatment, course of disease, and age, as

well as in EA and acupuncture. Having searched the related literature published in China and abroad, the present authors still cannot eliminate the potential of publication bias.

Conclusion and future research

Acupuncture has a good short-run therapeutic effect in treating FMS that is maintained for 1-3 months, with the first month having the best therapeutic effect. Therefore, the treatment of a patient with FMS for 1 month with acupuncture in conjunction with an anti-depressant drug and exercise therapy is recommended as the most favorable therapeutic effect.

In future research, the gold standard for acupoint selection rather than personal experiences, as well rigorous trials of equivalence or non-inferiority in comparison with Western Medicine should be first sought. A further research direction is the integration of acupuncture and Western Medicine such as an optimal selection of Western Medicine, acupoint selection and treatment course. Appropriate sham acupuncture and non-therapeutic or ineffective acupoints should be explored for placebos. Given that acupuncture works by different acupoint groupings (or prescriptions) to treat diseases, it should therefore be described as effective or ineffective that certain groups of acupoints contrast certain intervention measures. Thus, the single word 'acupuncture' is not recommended in the treatment of FMS.

Acupuncture is increasingly used as a traditional therapy in western countries to treat musculoskeletal disease.[40] We suggest that the diagnostic criteria proposed by the ACR in 2010[41] should be adopted in future research. Moreover, based on the CONSORT Statement, a rigorously designed multi-center RCT and a large practical sample should be implemented to assess the clinical therapeutic effect of FMS by acupuncture therapy.

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